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EXAMINER	
LANDAU, SHARMILA GOLLAMUDI	

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1611	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	09/913,752	FERCEJ TEMELJOTOV ET AL.	
	Examiner	Art Unit	
	Sharmila Gollamudi Landau	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 May 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *70-72 and 76-84* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *70-72, 76-84* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt of Amendments and Remarks filed 5/6/08 is acknowledged. Claims 1-69 and 73-75 stand cancelled. Claims **70-72, 76-84** are pending in this application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 70-72, 76-84 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 80 and claim 82 recite "at least about 42%" which does not have support in the specification as originally filed. Applicant does not have support for the term "at least" or the term "about". The range "at least 42%" encompasses any concentration over 42%. Example 1 incorporates clarithromycin in an amount of 43.47%; examples 2 and 3 in an amount of 42.01%; example 4 in an amount of 43.47%; and example 5 in an amount of 43.47%. Further, the term "about" encompasses any range below 42, which applicant does not have support for. It is noted that applicant does not provide any general range in the specification. However, applicant does have support for 42.01% and 43.47% clarithromycin.

Claim 80 recites "wherein the components are combined to allow the glycerol behenate to form the matrix and wherein the hydroxypropyl methylcellulose and the clarithromycin

component are dispersed within the matrix", does not have support in the specification as originally filed. It is noted that page 4, line 22 to page 5, line 5 discloses that the water-insoluble component [glyceryl behenate], the hydrophilic component, and the drug form the matrix.

New claim 84 is directed to weight percents that are not disclosed in the originally field specification or claims. The recitation "about 22%" glyceryl behenate and "about 17%" hydroxypropylmethylcellulose does not have support. Further, applicant does not have support for "at least about 43%". The range "at least 43%" encompasses any concentration over 43%. Example 1 incorporates clarithromycin in an amount of 43.47%; examples 2 and 3 in an amount of 42.01%; example 4 in an amount of 43.47%; and example 5 in an amount of 43.47%. Further, the term "about" encompasses any range below 43 including a concentration of, for instance, 41%. Applicant does not have support for this. It is noted that applicant does not provide any general range in the specification. However, applicant does have support for 42.01% and 43.47% clarithromycin.

If applicant contends there is support for the above limitations, applicant is requested to specify the page and line of said support. Applicant's attention is directed to MPEP 714.03, "Applicant should also specifically point out the support for any amendments made to the disclosure." Applicant has not done so.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 72, 76-78, 80-83 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 95/22319 to Briskin et al in view of Gibson et al (5,811,120). Regarding amended claim 82, METHOCEL and WO 98/42311 are relied upon as evidence.

Briskin teaches preparing pharmaceutical composition comprising up to 90% of an active agent, 1-75% of an extrusion aid including glyceryl behenate, hydrogenated vegetable oil, fats, fatty acid esters, fatty acids, etc. The composition further contains binding agents including polyvinylpyrrolidone (povidone K90), carboxymethylcellulose, and hydroxymethylcellulose (HMC) to retard release. See page 4-5. Briskin teaches an oral composition containing 43.4% clarithromycin, 5.5% povidone, 26% carbopol, 5% hydroxypropyl cellulose (an alkyl-substituted cellulose ether), 10% glyceryl behenate, and 10% microcrystalline cellulose. See table 1 on page 8. Specifically example 1b. Note that example 1b contains 5.5% povidone and 5% hydroxypropylcellulose, which comprises a total of 10.5% of the binder.

The composition is then formulated in to a tablet or capsule. See page 7, line 7. On page 6, the method of making the tablet is disclosed wherein the *all* the ingredients are blended

thoroughly, granulated, and then the particles are formed into tablets. Briskin discloses on page 5, lines 34-35 an enteric coating. Note that enteric coating is inherently acid resistant coating.

Briskin teaches the use of hydrophilic binders, specifically HMC and PVP (povidone) as the hydrophilic binder, however Briskin does not the use of hydroxypropylmethylcellulose (HPMC). Further, Briskin does not teach instant surfactant.

Gibson et al teach pharmaceutical formulations containing raloxifene. Gibson et al teaches the conventional additives in pharmaceutical formulations such as hydrophilic binders. Gibson teaches the term "hydrophilic binder" represents binders *commonly used in the formulation of pharmaceuticals*, such as ***polyvinylpyrrolidone (PVP)***, polyethylene glycol, sucrose, dextrose, corn syrup, polysaccharides (including acacia, tragacanth, guar, and alginates), gelatin, and cellulose derivatives (including ***hydroxypropyl methylcellulose, hydroxypropyl cellulose***, and sodium carboxymethylcellulose). See column 3, lines 50-60. Further, Gibson teaches the use of surfactants including sodium docosate. See column 3, lines 60-67. Further, the reference teaches that the preparation of the oral formulations is well known in the art such as direct compression. The process includes mixing the active with the hydrophilic binder and surfactant, which is then, milled if necessary, drying the granules, and compressing into tablets (col. 5, lines 10-15).

It would have been obvious of one of ordinary skill in the art at the time the invention was made to combine the teachings of Briskin et al and Gibson et al and utilize the instant hydrophilic binder (HPMC). One would have been motivated to substitute Briskin's hydrophilic binders (cellulose derivative HMC and Povidone) for instant cellulose derivative (HPMC) with a reasonable expectation of similar results since Gibson teaches that HPMC, HMC and Povidone

are conventional hydrophilic binders utilized in pharmaceutical compositions. Therefore, it is prima facie obvious for a skilled artisan to substitute one functional equivalent with another known functional equivalent with the expectation of similar results and success since the art establishes that both are hydrophilic and act as binders in the composition. The examiner points out that Briskin teaches the binder in a total weight percent of 10.5 (5.5% povidone and 5% hydroxypropylmethylcellulose). Thus, it is the examiner's position that the prior art's 10.5% reads on the claimed "***about*** 13%". It is noted that the term "about" is not defined in the specification to mean exactly. See MPEP 2111.01. Moreover, it is within the skill of an artisan to manipulate the amount of the binder, which is taught to retard the release in the composition. One would have been motivated to do so depending on the desired release rate.

Additionally, Gibson teaches the conventional use of surfactants such as instant sodium docusate in pharmaceutical compositions. Thus, the use of conventional additives in the preparation of pharmaceuticals is prima facie obvious.

Regarding claim 82, the combination of the Briskin and Gibson would provide a composition that forms a viscous layer since this is a natural property of HPMC. METHOCEL data sheet discloses METHOCEL of varying viscosities has the ability to form a gel layer. Further, it should be noted that HPC taught by Briskin also is capable of forming a viscous layer as evidenced by WO 98/42311.

Response to Arguments

Applicant argues that Briskin fails to appreciate the significance of forming a matrix with these components to facilitate the controlled release of clarithromycin. Applicant argues that although Briskin teaches a composition comprising clarithromycin, hydroxymethylcellulose, and

glycerol behenate, Briskin does not teach a matrix. Applicant argues the amounts and ratios of components used are all relevant to the resulting formulation. Applicant argues that 10% glyceryl behenate is less than the present invention of 21.5%. Applicant argues that Briskin only teaches 5% HPMC and the instant invention only uses over 17%. Applicant argues that mixing, sieving, and combining the instant components do not necessarily form a matrix. Applicant argues that Briskin teaches glyceryl behenate as an extrusion aid and not as a controlled release agent. Applicant argues that Gibson fails to remedy the deficiencies of Briskin because Gibson does not suggest a matrix formulation utilizing glyceryl behenate and hydroxypropyl methylcellulose in the amounts specified.

Applicant's arguments filed 5/6/08 have been fully considered but they are not persuasive. The claims are directed to a pharmaceutical composition and method of making a pharmaceutical composition comprising about 10-36% glycerol behenate; about 13-18% hydroxypropyl methylcellulose, dispersed within the matrix, and at least about 42% clarithromycin dispersed within a matrix. Independent claim 80 and 82 recite broad ranges and not the limited ranges applicant argues. Briskin discloses an oral composition containing 43.4% clarithromycin, 5.5% povidone, 26% carbopol, 5% hydroxypropylcellulose (an alkyl-substituted cellulose ether), 10% glyceryl behenate, and 10% microcrystalline cellulose. See table 1 on page 8.

Firstly, it is noted that applicant argues that Briskin does not teach a matrix; however the examiner respectfully disagrees. The instant application discloses on page 7 that the instant invention is made by mixing all the ingredients together, sieving, and compressing to form a tablet. The examiner points out that Briskin discloses on page 6, the method of making the tablet

wherein the *all* the ingredients are blended thoroughly, granulated, and then the particles are formed into tablets. Therefore, since Briskin teaches combining all the components, a matrix would necessarily form. Applicant has not provided any evidence to the contrary.

Applicant argues that the ratio of the components forms the structure.

Applicant claims about10-36% and example 1 in Briskin utilizes 10% glyceryl behenate, i.e. the claimed amount. The fact that the prior art utilizes glyceryl behenate for a different purpose does not provide a patentable distinction to the instant invention. The fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). Regarding the hydrophilic polymer, Briskin teaches 5.5% povidone and 5% HPC combined with 10% glyceryl behenate. Thus Briskin teaches the hydrophilic polymer in a total amount of 10.5%. 10.5% renders **about** 13% obvious and applicant has not provided any unexpected results rebutting the examiner's position. Therefore, Briskin teaches the instant amount of the components and teaches similar hydrophilic components (PVP, HPC, and HPMC all swell in the presence of water to form a viscous material). Thus, one would reasonably assume that not only would a matrix form but a viscous layer would form. The examiner has made a reasonable rationale and the burden has shifted to the examiner to rebut this position with evidence. Applicant has not provided such evidence.

Applicant argues that Briskin fails to provide a motivation to use hydrophilic polymers in conjunction with fatty components.

Briskin clearly discloses the use of hydrophilic binders such as hydroxypropylcellulose and polyvinylpyrrolidone in combination with glyceryl behenate. Therefore, the only deficiency in Briskin is the use of the instant hydrophilic component.

Applicant argues that Gibson and Evenstad do not remedy the deficiencies of Briskin. Applicant argues there is no motivation to experiment with hydrophilic polymers as fatty components to provide a matrix. Applicant argues the examiner has relied upon impermissible hindsight.

The examiner has discussed the merits of Briskin above. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). First, it is noted that Briskin discloses the use of a hydrophilic polymer, in particular hydroxypropylcellulose (HPC), in combination with a fatty component. Additionally, Briskin discloses the use of various hydrophilic binders including HPC to retard release. See page 5, lines 17-20. Therefore, Gibson is only relied upon to teach the functional equivalency of PVP, HPC, and HPMC. Gibson establishes that all the polymers are hydrophilic and function as binders. Briskin itself suggests the combination of a hydrophilic polymer and a fatty component. Applicant has not addressed this argument.

Applicant argues that simply substituting one ingredient for another will not result in the instant controlled release.

It is noted that applicant discloses on pages 5 to 6 that all alkyl-substituted cellulose ethers are suitable for the hydrophilic component. It is pointed out that Briskin teaches the use of PVP or HPC as binders that retard release. Thus, Briskin not only suggests the use of these hydrophilic binders but Briskin exemplifies it. Further, Gibson reiterates that PVP, HPC, and HPMC are all hydrophilic binders and thus a skilled artisan would expect similar results. Applicant has not provided any evidence that these polymers are not functional equivalents.

Applicant argues that HPMC is not used as a binder but as a rate controlling polymer.

Applicant's attention is directed to page 5, lines 17-20 in which Briskin teaches the use of binders such as PVP and HPC is to retard release. Therefore, a hydrophilic binder functions to retard release rate. Further, regardless of the viscosity of the HPMC, it will necessarily form a viscous layer. Note METHOCEL as art of interest.

Therefore, it is the examiner's position that Briskin and Gibson render the instant invention obvious.

Claims 70-71 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 95/22319 to Briskin et al in view of Gibson et al (5,811,120) as evidenced by METHOCEL and WO 98/42311 for claim 82, in further view of Evenstad et al (5,126,145).

The disclosure of Briskin and Gibson have been set forth above. Briskin teaches the use of HPC and PVP as the hydrophilic *binder* and Gibson teaches the use of PVP, HPC or HPMC as the hydrophilic *binder*.

The references do not specify the viscosity of HPMC.

Evenstad teaches a controlled release tablet. Evenstad teaches the use of high viscosity HPMC to provide sustain release whereas a water-soluble pharmaceutical binder such as HPMC having binding properties has a much lower viscosity; typically a viscosity of less than 100 cps such as METHOCEL E15. See column 3, lines 5-67. METHOCEL E15 has a viscosity of 12-18 cps. Note this reads on the recitation "up to about 40 cP".

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Briskin, Gibson, and Evenstad and specifically utilize a low viscosity HPMC. One would have been motivated to do so since Evenstad teaches high viscosity HPMC is useful for its sustaining action and low viscosity HPMC is useful for its binding properties. Therefore, a skilled artisan would have been motivated to utilize a low viscosity HPMC with a reasonable expectation of similar results since both Briskin and Gibson teach the use of the cellulose derivative for its binding property and Evenstad teaches the low viscosity cellulose derivative provide this function.

Response to Arguments

Applicant argues that Evenstad fails to remedy the deficiencies of Briskin. Applicant argues that Evenstad merely disclosing a controlled release tablet and the use of low viscosity HPMC, a viscosity less than 100 cps.

Applicant's arguments filed 5/6/08 have been fully considered but they are not persuasive. The merits of Briskin have been disclosed above and incorporated herein. Evenstad teaches METHOCEL E15 which has a viscosity of 12-18 cps and reads on instant recitation "up to about 40 cP". Although applicant argues against the prior art due to its use of the term

"binder", it is noted that the claimed viscosity range is that of the prior art's. Therefore, it is the examiner's position that Briskin, Gibson, and Evenstad render the instant invention obvious.

Claim 79 is rejected under 35 U.S.C. 103(a) as being unpatentable over WO 95/22319 to Briskin et al in view Gibson et al (5,811,120) as evidenced by METHOCEL and WO 98/42311 for claim 82 in further view of Khan et al (5,656,296).

The disclosures of Briskin and Gibson have been set forth above.

Briskin teaches the composition may be coated with an enteric coating or other coatings. See page 5, lines 30-35.

The combined references do not teach a coating comprising the instant polymers.

Khan teaches a dual control sustained release drug delivery system. Khan teaches the delivery system is coated with a coating layer comprising a water insoluble polymer and water-soluble film forming polymers including cellulose derivatives such as hydroxypropylcellulose, hydroxypropyl-methylcellulose, hydroxypropylmethylcellulose phthalate, sodium carboxymethylcellulose, and the like, and mixtures thereof. See column 6, lines 30-60.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Briskin, Gibson, and Khan and utilize a coating layer comprising a mixture of polymers such as HPMC and HPC. One would have been motivated to do so to provide a sustained release effect. Further, a skilled artisan would have reasonably expected success since Briskin teaches the use of various coating layer.

Response to Arguments

Applicant argues that the controlled release properties of the present invention are imparted by the hydrophilic lipid matrix, and not by the presence of a coating. Thus, the presence

of a sustained release coating in the disclosure of Khan does not remedy the deficiencies of Briskin and Gibson.

Applicant's arguments filed 5/6/08 have been fully considered but they are not persuasive. The merits of Briskin and Gibson have been discussed above and incorporated herein. Since applicant has not specifically argued the merits of the instant rejection, the rejection is maintained.

Claims 70-72, 76-84 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 98/42311 to Akiyama et al in view WO 98/14176 to Farah et al (US equivalent 6,194,005 is used as the translation). It should also be noted that applicant has not perfected priority.

Akiyama et al teach a gastrointestinal mucosa adherent matrix adapted to stay long in the gastrointestinal tract for sustained drug release. The gastrointestinal mucosa-adherent matrix which is solid at ambient temperature includes a matrix in which each matrix particle containing a polyglycerol fatty acid ester and/or a lipid and an active ingredient has a coating layer comprising or containing the viscogenic agent.

Examples of viscogenic agent include polymers containing carboxyl groups or salts thereof, cellulose ethers, polyethylene glycols having molecular weights not less than 200,000, and naturally-occurring mucous substances. The preferable viscogenic agents are those having a viscosity in the range of 3 to 50,000 cps, preferably 10 to 30,000 cps, and more preferably 15 to 30,000 cps as a 2 percent by weight aqueous solution thereof at 20.degree. C. Cellulose ethers taught include hydroxymethylcellulose. See page 17, lines 10-35 and page 18, line 36. **The**

viscogneic agent is taught in a preferable amount of 1-20%. See page 19, lines 10-15. HMC is taught on page 18.

The matrix may be made of polyglycerol fatty acid ester be about 15 to 80.degree. C., preferably about 30 to 75.degree. C. and more preferably about 45 to 75.degree. C or lipids having a melting point of 40 to 120.degree. C., preferably 40 to 90.degree. C. The polyglycerol fatty acid esters include behenyl glycerides and the lipids include glycerol fatty acid esters wherein behenic acid is taught as a fatty acid. See page 8, lines 1-5, page 10, and page 12, lines 8-36 .**The lipid is utilized in an amount of 5-98%.**

The active includes antimicrobial substance and preferably **clarithromycin**. See page 14, lines 25-30 and page 15, lines 1-2. The active is used in an amount of 0.005-95% and preferably about 10 to about 50%. See page 26, lines 12-20.

The solid composition may be coated with a coating material including hydroxypropylmethylcellulose phthalate. See page 22, lines 15-25 and page 23, lines 30-35. The solid dosage form includes tablets. See page 25, line 14. The composition includes surfactants. See page 29, lines 1-15. The examples provide the method of making the composition.

Akiyama does not specify the glycerol fatty acid ester.

Farah teaches a method for preparing a pharmaceutical composition with modified release of the active principle, comprising a matrix as lipid matrix agent, of an ester of behenic acid and of alcohol. The alcohol is advantageously chosen from the group comprising **glycerol, polyglycerol**, propylene glycol, propylene glycol in combination with ethylene oxide and polyethylene glycol. These matrix agents exhibit the advantage of having a melting point of greater than 50.degree. C., which prevents them from disintegrating at the compression

temperature. Furthermore, this melting point is greater than the internal temperature of the human body (37.degree. C.), which allows the lipid agent to have a more pronounced matrix behavior. The lipid is used in an amount of **1-15%.** See column 4, lines 10-55. **Glycerol behenate is the preferred lipid for the matrix.**

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Akiyama and Farah and utilize glycerol behenate in Akiyama's composition. One would have been motivated to do so with a reasonable expectation of success and similar results since Akiyama teaches the use of lipids with a melting point of 40-120 degrees C such as glycerol fatty acid esters for the matrix and Farah teaches glycerol behenate may be used to form a lipid matrix in sustained release composition. Further, Farah teaches the esters of behenic acid and alcohol may used wherein the alcohol may be glycerol or polyglycerol. Thus, Farah teaches that both the polyglycerols of fatty acid esters and glycerol of fatty acid esters may be used to form the matrix and therefore establishes the functional equivalency. Therefore, it would have been obvious to substitute one lipid matrix forming material with another similar lipid matrix forming material.

Regarding claim 84, Akiyama teaches the active in an amount of about 0.005-95%, preferably about 1-95%, more preferably about 10-95%, and most preferably about 10-50%. This range overlaps the instant range of at least about 43%. Akiyama incorporates viscogenic agent is incorporated preferably amount of the viscogenic agent is 1-20%, which encompasses "about 17%". Thus, it is within the skill of an artisan to manipulate the concentration based on the general range provided by the prior art absent evidence of the unexpectedness of the claimed range. One would have been motivated to do so during routine optimization Further, Akiyama

incorporates the lipid in an amount of 5-98% and Farah teaches 1-15%. Thus, it is within the skill of an artisan to manipulate the concentration based on the general range provided by the prior art and absent evidence of unexpectedness of the instant amount. One would have been motivated to do so depending on the desired release profile.

Response to Arguments

Applicant argues that Akiyama is not related to sustained release and not a dual matrix.

Applicant's arguments filed 5/6/08 have been fully considered but they are not persuasive. Applicant's attention is directed to page 19, lines 12-20. Akiyama discloses,

> "When, for example, the viscogenic agent is dispersed in a ***matrix*** comprising the polyglycerol fatty acid ester and/or lipid, the amount of the viscogenic agent is about 0.005 to about 95 weight %, preferably about 0.5 to about 30 weight %, and more preferably about 1 to about 25 weight %, and for still better result, about 1 to about 20 weight % based on the total weight."

Thus, the reference clearly teaches a matrix comprising a lipid and hydrophilic polymer ("viscogenic agent").

Applicant argues that clarithromycin and HPMC are merely listed.

Akiyama teaches the viscogenic agent, which is a critical component of the invention, may be selected from any agent that is capable of swelling in the water. See page 17, lines 10-15. The reference teaches the polymer may be a naturally occurring material or synthetic polymers. HPMC and HPC are among the natural occurring polymers taught. See page 18, lines 35-36. Thus, Akiyama is not limited to L-HPC. It should be noted that "[d]isclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments." *In re Susi*, 440 F.2d 442, 169 USPQ423 (CCPA 1971). Further, the preferable amount of the viscogenic agent is 1-20%, which overlaps the instant range 13-18%.

Applicant's attention is directed to MPEP 2144.05. "In the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a prima facie case of obviousness exists. In re Wertheim, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); In re Woodruff, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990)

Regarding clarithromycin, page 15, line 2 discloses Akiyama's preference for clarithromycin. The drug is incorporated, preferably, in an amount of about 0.005-95%, preferably about 1-95%, more preferably about 10-95%, and most preferably about 10-50%. This range overlaps the instant range of at least about 42% or 43%. Again, applicant's attention is directed to MPEP 2144.05.

Applicant argues that the aim of Akiyama is to keep the formulation for a longer time in the stomach for healing of ulcers, and thus is not targeted or intended for sustained release as with the present invention. Dissolution profiles are not discussed and Farah does not remedy this deficiency.

Clearly, Akiyama teaches a sustained release device since the inventive thrust is directed to extending the gastroduodenal residence time, i.e. sustained release.

Applicant argues that Farah does not remedy the deficiency of Akiyama. Applicant argues that Farah teaches lower amounts of the lipid. The reference teaches 1-15% versus 21.5%.

First, it is noted that Akiyama suggests the use of glyceryl behenate. The reference teaches the use of fatty acid glycerol esters wherein the fatty acid may be behenic acid. See page 12. Further, Akiyama teaches the incorporating the lipid in an amount of 5-98%. Second, claims 80 and 82 are directed to glyceryl behenate in an amount of 10-36% and not 21.5%. Again, the prior art's range overlaps with the instant range. Regarding claim 84, absent evidence of

unexpectedness of the instant amount, it is the examiner's position that it is within the skill of an artisan to manipulate the amount of the lipid based on the desired release profile since Akiyama teaches 5-98%.

Therefore, it is the examiner's position that Akiyama and Farah render the instant invention obvious.

Conclusion

This action is made non-final.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharmila Gollamudi Landau whose telephone number is (571) 272-0614. The examiner can normally be reached on Monday- Friday (8:30-6).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on 571-272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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